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FOLEY & LARDNER LLP
150 EAST GILMAN STREET
P.O. BOX 1497
MADISON, WI 53701-1497

EXAMINER	
CROW, ROBERT THOMAS	
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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/773,753	HAMERS ET AL.	
	Examiner	Art Unit	
	Robert T. Crow	1634	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *07 March 2008*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-24 and 32-37* is/are pending in the application.

4a) Of the above claim(s) *12-24* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-11 and 32-37* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Continued Examination Under 37 CFR 1.114

1. A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 7 March 2008 has been entered.

Status of the Claims

2. This action is in response to papers filed 7 March 2008 in which claims 1, 6, 32, and 37 were amended, no claims were canceled, and no new claims were added. All of the amendments have been thoroughly reviewed and entered.

The previous rejections under 35 U.S.C. 102(a,e) and 35 U.S.C. 103(a) not reiterated below are withdrawn in view of the amendments. Applicant's arguments have been thoroughly reviewed and are addressed following the rejections necessitated by the amendments.

Claims 1-11 and 32-37 are under prosecution.

Claim Rejections - 35 USC § 102

3. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.
> (e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

4. Claims 1-6, 9, and 32-37 are rejected under 35 U.S.C. 102(a,e) as being anticipated by Fish (PCT International Publication No. WO 02/054052 A1, published 11 July 2002).

Regarding claim 1, Fish teaches a modified substrate. In a single exemplary embodiment, Fish teaches Figures 2C-D, which show substrate surface 20 having a binding agent, in the form of the double stranded molecule formed by hybridization of oligonucleotide probe molecule 16 to analyte 15a, attached (second embodiment, pages 18-19 and page 50, lines 1-5), wherein the attachment of the binding agent (i.e., 16) to the surface is covalent (pages 42-43). The binding agent is a biological molecule because the molecule is an oligonucleotide (page 50, lines 1-5) hybridized to a target DNA (page 50, lines 1-2). Thus, the claimed biomolecule is the double stranded (i.e., target/probe) DNA, which is a biological molecule, that is covalently linked to the surface. Paragraphs 0042-0044 of the instant specification recite embodiments wherein the biomolecules include, but are not limited to, DNA sequences. Further, a review of the specification yields no teaching excluding double stranded DNA sequences; thus, the claim has been given the broadest reasonable interpretation consistent with the teachings of the specification regarding a "biomolecule" (*In re Hyatt*, 211 F.3d1367, 1372, 54 USPQ2d 1664, 1667 (Fed. Cir. 2000) (see MPEP 2111 [R-1]). Figures 2C-D of Fish further comprises nanotube 26 (i.e., a nanocylinder), having oligonucleotide 26b attached, which hybridizes to a single stranded portion of analyte 15a (second embodiment, pages 18-19). The hybridization is the specific binding between the overhang of the first biomolecule (i.e., the overhang on 15a of double stranded 16/15a) and complementary biomolecule 26b.

Fish also teaches the covalent attachment of the oligonucleotides 26a to the nanotube; namely, Figure 2F, which illustrates covalent linkage of amino terminal oligonucleotides to the end of the nanotubes (page 18, last two lines –page 19).

Regarding claims 2-3, Fish teaches the substrate of claim 1, wherein the nanocylinder is a carbon nanotube (page 18, second full paragraph).

Regarding claim 4, Fish teaches the substrate of claim 1, wherein the nanocylinder is a gold nanorod; namely, 26 is a conductive particle (page 18, second full paragraph), wherein the electrically

readable (i.e., conductive) particles are metal nanowires having gold as the preferred material (page 34, second full paragraph).

Regarding claim 5, Fish teaches the substrate of claim 1, wherein the covalently linked biomolecules are oligonucleotide sequences; namely, the biomolecule, which comprises analyte 15a hybridized to oligonucleotide probe 16 (pages 18-19 and lines 1-5 of page 50), and oligonucleotide 26b is on nanotube 26 (pages 18-19).

Regarding claim 6, Fish teaches the substrate of claim 1, the covalently linked surface biomolecule comprises a singles stranded sequence, and the complementary biomolecule covalently linked to the nanocylinder comprises a complementary single stranded sequence; namely, the covalently linked biomolecule comprising analyte 15a hybridized to oligonucleotide probe 16 has a single stranded overhang (i.e., sequence) that hybridizes to single stranded 26b (Figures 2C-D , pages 18-19 and lines 1-5 of page 50).

It is noted that claim 6 is drawn to a molecule comprising single stranded oligonucleotide **sequences**, not to single stranded oligonucleotide **molecules**. Thus, the double stranded portion of the covalently immobilized double stranded 15a/16 is encompassed by the open language "comprising" of the instant claim.

Regarding claim 9, Fish teaches the substrate of claim 1, wherein the substrate is glass; namely, a glass plate (Example 2, page 56).

Regarding claim 32, Fish teaches a nanocylinder bridge. In a single embodiment, Fish teaches Figure 2D, comprising first surface 20 having a biomolecule in the form of binding agent 16 hybridized to analyte 15a immobilized thereon (second embodiment, pages 18-19), wherein the attachment of the binding agent (i.e., molecule) to the surface is covalent (pages 42-43). Figure 2D further comprises second surface 12 having a second biomolecule in the form of binding agent 16a hybridized to analyte 15b and immobilized thereon (second embodiment, pages 18-19), wherein the attachment of the binding agent (i.e., molecule) to the surface is covalent (pages 42-43). The binding agents are biological

molecules; namely, probes 16 and 16a are oligonucleotides (page 50, lines 1-5), which bind to analytes 15a and 15b, which are DNAs (page 50, lines 1-2). Thus, the claimed biomolecules are the two double stranded (i.e., target/probe) DNAs 16/15a and 16a/15b that are covalently linked to the surface. Paragraphs 0042-0044 of the instant specification recite embodiments wherein the biomolecules include, but are not limited to, DNA sequences. Further, a review of the specification yields no teaching excluding double stranded DNA sequences; thus, the claim has been given the broadest reasonable interpretation consistent with the teachings of the specification regarding a "biomolecule."

Fish also teaches the covalent attachment of the oligonucleotides 26a and 26b to the nanotube; namely, Figure 2F, which illustrates covalent linkage of amino terminal oligonucleotides to the opposite ends of the nanotubes (page 18, last two lines –page 19). The hybridization between the overhangs of the double stranded nucleic acids with the nucleic acids on the ends of the nanocylinder described above thus forms a bridge with carbon nanotube 26 forming the bridge between surfaces 21 and 20.

Regarding claim 33, Fish teaches the bridge of claim 32, wherein the nanocylinder is a carbon nanotube (page 18, second full paragraph).

Regarding claim 34, Fish teaches the bridge of claim 32, wherein the biomolecules on the nanotube are on opposite ends and are covalently attached; namely, Figure 2F, which illustrates covalent linkage of amino terminal oligonucleotides to the opposite ends of the nanotubes (page 18, last two lines –page 19).

Regarding claim 35, Fish teaches the bridge of claim 32. Fish also teaches that analytes 15a and 15b both must be present (page 19, first paragraph), which is interpreted to mean that they are different sequences. Fish also teaches the covalently linked oligonucleotides 26a and 26b on nanotube 26, which are interpreted as different sequences as a result of their different numerical labels. Fish also teaches covalently linked oligonucleotides 16a and 16 on the two surfaces, which are also interpreted as different sequences as a result of their different numerical labels. Therefore, oligonucleotides 15a, 15b, 26a, 26b, 16,

and 16a of Figure 2D are each interpreted as being different sequences, and meet the limitations of the instant claim.

Regarding claim 36, Fish teaches the bridge of claim 32, wherein the first and second surfaces are metals; namely, silicon wafers (Example 1, page 56).

Regarding claim 37, Fish teaches a patterned surface; namely, the electrode array of Figure 9 (sixth embodiment, pages 26-28). Turning to Figure 9, electrodes 30-34 are on a lower insulator substrate, and electrodes 40-42 are on an upper insulator substrate. Each intersection of electrodes performs a different assay to detect different analytes, and each intersection comprises binding agents and electrically readable particles (page 27, lines 1-5). Fish further teaches the patterned surface comprises first surface 20 having a biomolecule in the form of binding agent 16 hybridized to analyte 15a immobilized thereon (second embodiment, pages 18-19), wherein the attachment of the binding agent (i.e., molecule) to the surface is covalent (pages 42-43). Figure 2D further comprises second surface 12 having a biomolecule in the form of binding agent 16a hybridized to analyte 15b immobilized thereon (second embodiment, pages 18-19), wherein the attachment of the binding agent (i.e., molecule) to the surface is covalent (pages 42-43). The binding agents are biological molecules; namely, probes 16 and 16a are oligonucleotides (page 50, lines 1-5), which bind to analytes 15a and 15b, which are DNAs (page 50, lines 1-2). Thus, the claimed biomolecules are the two double stranded (i.e., target/probe) DNAs 16/15a and 16a/15b that are covalently linked to the surface. Paragraphs 0042-0044 of the instant specification recite embodiments wherein the biomolecules include, but are not limited, to DNA sequences. Further, a review of the specification yields no teaching excluding double stranded DNA sequences; thus, the claim has been given the broadest reasonable interpretation consistent with the teachings of the specification regarding a "biomolecule."

Figure 2D further comprises nanotube 26 (i.e., a nanocylinder), having oligonucleotides 26a and 26b attached, which hybridizes to their respective analyte DNAs (second embodiment, pages 18-19). Fish also teaches the covalent attachment of the oligonucleotides 26a and 26b to the nanotube; namely, Figure

2F, which illustrates covalent linkage of amino terminal oligonucleotides to the opposite ends of the nanotubes (page 18, last two lines –page 19). The hybridization between oligonucleotides 26a and 26b and analytes 15a and 15b thus forms a bridge with carbon nanotube 26 forming the bridge between surfaces 21 and 20.

While Fish does not explicitly teach a **plurality** of nanotubes attached to the surface through biomolecular interactions, Fish does teach a plurality of pairs of opposed electrode pairs that enable detection of several different analytes in any sample (page 15, last 5 lines of the first paragraph). Therefore, during use of the substrate, more than one nanotube is arranged on the surface in the pattern predetermined by the placement of biomolecules 116. Further, Figures 2C-D each show a plurality of binding agents 16 and 16a on their respective pairs of electrodes. While only one nanotube is shown bound in Figures 2C-D, Fish does teach specifically bound particles (i.e., a plurality) bound to an electrode (i.e., one electrode; page 17, lines 6-8). Thus, during use of the substrate, more than one nanotube is arranged on the surface at each electrode in the pattern predetermined by the placement of biomolecules 116.

Response to Arguments

Applicant's arguments filed 7 March 2008 (i.e., the "Remarks") have been fully considered but they are not persuasive for the reason(s) listed below.

A. Applicant argues on page 10 the Fish does not anticipate independent claims 1, 32, and 32 as amended because the claims require attachment of the nanocylinder to the surface through specific binding of the biomolecule on the surface and the biomolecule linked to the nanocylinder wherein the attachment is not through a third biomolecule. Further, on page 9 of the Remarks, Applicant cites paragraphs 0013, 0037, 0042-0044, and 0060-0062 for support of the amendments.

However, as noted above, paragraphs 0042-0044 of the instant specification recite embodiments wherein the biomolecules include, but are not limited to, DNA sequences. Further, a review of the

specification, in particular of cited paragraphs 0013, 0037, 0042-0044, and 0060-0062, yields no teaching excluding double stranded DNA sequences. Thus, the claimed biomolecules are interpreted as the double stranded molecules 16/15a and 16a/15b of Fish, which have single stranded overhangs on strands 15a and 15b, which specifically bind with biomolecules 26b and 26a on the nanocylinder of Figures 2C-D. In addition, it is also noted that claim 6 is drawn to a molecule comprising single stranded oligonucleotide **sequences**, not to single stranded oligonucleotide **molecules**. Thus, the double stranded portion of the covalently immobilized double stranded 15a/16 is encompassed by the open language "comprising" of the instant claim. Fish thus anticipates the claims as described above, and the claim has been given the broadest reasonable interpretation consistent with the teachings of the specification regarding a "biomolecule."

B. Applicant further argues on page 11 of the Remarks that Fish does not each direct (i.e., specific) binding without a third biomolecule.

However, as noted above, the claimed biomolecules are interpreted as the double stranded molecules 16/15a and 16a/15b of Fish, which have single stranded overhangs on strands 15a and 15b, which specifically bind with biomolecules 26b and 26a on the nanocylinder of Figures 2C-D, and the claim has been given the broadest reasonable interpretation consistent with the teachings of the specification regarding a "biomolecule" as detailed above.

C. In addition, it is noted that Applicant's amendments result in the exclusion of the embodiments of the invention illustrated in each of Figures 3-4 because each of Figures 3-4 show attachment of the nanocylinder to the surface using a third biomolecule (e.g., rhodamine labeled avidin in Figure 3 and molecule "A" in Figure 4). This is mentioned solely for Applicant's convenience and does not affect the examination of the claims.

5. Claims 1-3 and 5-9 are rejected under 35 U.S.C. 102(b) as being anticipated by Braun et al (PCT International Publication No. WO 99/04440, published 28 January 1999).

Regarding claim 1, Braun et al teach a modified substrate. In a single exemplary embodiment, Braun et al teach an interface component, which is an electrode (page 7). An oligonucleotide is attached to the surface of the electrode, and is used as a linker for binding to a nucleotide-chain end segment of a fiber (Figure 1B and page 22). This oligonucleotide linker hybridizes (i.e., to a complementary sequence; page 9, definition of a "linker") to complementary sequences on a fiber (page 15). Oligonucleotides are biomolecules, and the fiber has nucleotide chains at each of the ends of a carbon nanotube (page 32, second paragraph), which is a nanocylinder. Thus, the hybridization that connects the substrate bound oligonucleotide biomolecule to the nanocylinder-bound complementary nucleic acid biomolecule is the specific binding of the instant claim, and occurs without the use of a third biomolecule. The oligonucleotides are covalently linked to the surface and the nanocylinder; namely, each of the biomolecules is bound to the respective substrate or nanocylinder, and Braun et al teach binding is covalent (page 5, definition of "binding").

Regarding claims 2-3, Braun et al teach the substrate of claim 1, wherein the nanocylinder is a carbon nanotube (page 32, second paragraph).

Regarding claim 5, Braun et al teach the substrate of claim 1, wherein the both of the biomolecules are oligonucleotide sequences; namely, the linker on the electrode is an oligonucleotide linker that hybridizes (i.e., to a complementary sequence; page 9, definition of a "linker") to complementary sequences on a fiber (page 15), and the fiber has nucleotide chains at each of the ends of a carbon nanotube (page 32, second paragraph).

Regarding claim 6, Braun et al teach the substrate of claim 1, wherein the both of the biomolecules are single stranded oligonucleotide sequences; namely, the linker is a single stranded nucleic acid (page 9) and the nucleotide chains at each of the ends of a carbon nanotube is also single stranded (page 5).

Regarding claim 7, Braun et al teach the substrate of claim 1, wherein the biomolecule covalently linked the surface and the complementary biomolecule form a protein ligand pair; namely, in an

embodiment alternative to that presented for claim 1 above, Braun et al teach the linker molecule and the molecule on the nanocylinder form an antibody-antigen pair (page 9). Antibodies are proteins, and the antigens are ligands to antibodies.

Regarding claim 8, Braun et al teach the substrate of claim 7, wherein the biomolecule covalently linked to the surface comprises avidin, and the complementary biomolecule covalently linked to the nanocylinder comprises biotin; namely, Braun et al teach the linker molecule and the molecule on the nanocylinder form an avidin-biotin pair (page 9).

Regarding claim 9, Braun et al teach the substrate of claim 1, wherein the substrate is a metal; namely, the interface component, which is an electrode (page 7), is made of metal (page 24, last paragraph).

Claim Rejections - 35 USC § 103

6. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

7. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

8. Claims 1 and 7-8 are rejected under 35 U.S.C. 103(a) as obvious over Fish (PCT International Publication No. WO 02/054052 A1, published 11 July 2002).

It is noted that this rejection draws upon an embodiment of claim 1 that is different that the embodiment described above under 35 USC 102(a,e). The specific limitations of claim 7 are noted parenthetically in the rejection.

Regarding claim 1 and 7, Fish teaches a modified substrate. In a single exemplary embodiment that is different from the embodiment described above under 35 USC 102(a,e), Fish teaches Figure 3B (third embodiment, pages 19-20), which shows the surface of electrode 31, which is a substrate, having analyte analog 317 bound thereon. Fish defines an analyte analog as a chemically modified analyte, and that the analyte is a protein (page 1); thus, 317 is a chemically modified protein (i.e., claim 7), which is a biomolecule. Fish also teaches the molecules are bonded on the surface using covalent bonds (page 43). Figure 3B further shows particle 127, wherein particle 127 is electrically readable (page 17), and the electrically readable (i.e., conductive) particle is a nanotube (page 34, second full paragraph), which is a nanocylinder.

Figure 3B also shows nanocylinder (i.e., particle) 127 bearing structure 115, which is bound to protein 317 (page 20) through structure 115. Thus, structure 115 is a ligand for protein 317 (i.e., claim 7) because structure 115 binds to protein 317 (i.e., claim 7), without the use of a third biomolecule to attach the molecule 115 on nanocylinder 127 to protein 317.

Fish does not explicitly teach that molecule 115 of Figures 3A-B is a biomolecule, or that molecule 115 is covalently bound to nanocylinder 127.

However, Fish teaches structure 115 is in antibody in a different embodiment (e.g., page 15, last paragraph), and that 115 is a binding agent (page 16, end of first paragraph). Fish also teaches that antibodies are attached to nanoparticles in Figure 3A-B (pages 47-48), and that nanotubes are functionally equivalent conductive particles (page 11, first 10 lines). In addition, Fish also teaches the covalent attachment of molecules is the most stable and strongest method of attachment (page 43, fist full

paragraph). Thus, Fish teaches the known technique of binding antibodies (i.e., proteins) to the nanoparticles and covalent attachment of molecules to surfaces.

It would therefore have been obvious to a person of ordinary skill in the art at the time the claimed invention was made that the embodiment depicted in Figures 3A-B could have been modified such that the competition assay of Figures 3A-B would utilize the known technique of having an antibody for structure 115 in accordance with the numbering used in the teachings of Fish. In addition, it would also have been obvious to the ordinary artisan that the conductive nanoparticle 127 could be modified to be the known functionally equivalent nanocylinder of Fish. It would further have been obvious to the ordinary artisan that that covalent attachment of the antibody 115 to nanocylinder 127 would have the added advantage of utilizing the most stable and strongest method of attachment (page 43, fist full paragraph). The modifications use known techniques to predictably provide (1) an assay having in a viable partner, in the form of an antibody, for the competitive assay and (2) attachment of the antibody to the functionally equivalent nanocylinder using (3) covalent attachment, and thus would have been obvious to the ordinary artisan at the time the claimed invention was made.

Regarding claim 8, the substrate of claim 1 is discussed above.

Fish does not explicitly teach the analyte analog is immobilized to the electrode using streptavidin.

However, Figures 3A-B depict an immunoassay. In the section on pages 47-49 labeled "Immunoassays," Fish specifically teaches biotinylated molecules (i.e., antibodies) are immobilized to the first surface (i.e., of the electrode) by binding to streptavidin, which has the added advantage that streptavidin spontaneously adsorbs to the surface of the electrode, thus simplifying preparation of the surface for immobilization. Thus, Fish teaches the known technique of immobilizing molecules to electrodes using Streptavidin.

It would therefore have been obvious to a person of ordinary skill in the art at the time the claimed invention was made that the first biomolecule could have been modified with biotin for

attachment to a streptavidinated electrode (i.e., the first surface) in accordance with the teachings of Fish to arrive at the instantly claimed surface comprising a streptavidin with a reasonable expectation of success. The ordinary artisan would have been motivated to make such a modification because said modification would have resulted in a modified substrate having the added advantage of simplified preparation of the surface for immobilization as explicitly taught by Fish (page 48). In addition, it would have been obvious to the ordinary artisan that the known technique of using the streptavidinated electrode of Fish could have been used to immobilize analyte analog 317 of Fish with predictable results because the known technique of using the streptavidinated electrode of Fish predictably result in stable association of the analog to the electrode surfaces.

With regards to the biotinylation of the nanocylinder, while Fish does not explicitly teach the antibody on the nanoparticle is biotinylated, Fish does teach the use of biotinylated antibodies (page 48). In addition, Fish also teaches the electrically readable (i.e., conductive) particles are metal nanowires having gold as the preferred material (page 34, second full paragraph), and that streptavidin spontaneously coats gold and is readily bound by biotin (page 48).

It would therefore have been obvious to a person of ordinary skill in the art at the time the claimed invention was made that in the embodiment of claim 7 wherein a nanocylinder is used, the functionally equivalent gold nanocylinder could have also been used. It would also have been obvious that attachment of antibody 115 (i.e., claim 7 above) could have utilized a biotinylated antibody by coating the gold nanocylinder with streptavidin in accordance with the teachings of Fish to arrive at the instantly claimed nanocylinder comprising a biotin with a reasonable expectation of success. The ordinary artisan would have been motivated to make such a modification because said modification would have resulted in a nanocylinder also having the added advantage of simplified preparation of the surface for immobilization as explicitly taught by Fish (page 48). In addition, it would have been obvious to the ordinary artisan that the known technique of using the streptavidinated gold surface of Fish could have been used to immobilize biotinlyated antibody 115 on the gold nanocylinder of Fish with

predictable results because the known technique of using the streptavidinated gold of Fish predictably results in stable association of a biotinlyated antibody to the gold surface.

9. Claims 1 and 10-11 are rejected under 35 U.S.C. 103(a) as being unpatentable over Fish (PCT International Publication No. WO 02/054052 A1, published 11 July 2002) in view of Strother et al (J. Am. Chem. Soc., vol. 122, pages 1205-1209 (2000)).

It is noted that this rejection applies to claim 1 to the extent that it is drawn to the embodiments of dependent claims 10-11.

Regarding claims 10-11, Fish teaches the modified substrate of claim 1. In a single exemplary embodiment, Fish teaches Figures 2C-D, which show substrate surface 20 having a binding agent, in the form of the double stranded molecule formed by hybridization of oligonucleotide probe molecule 16 to analyte 15a, attached (second embodiment, pages 18-19 and page 50, lines 1-5), wherein the attachment of the binding agent (i.e., 16) to the surface is covalent (pages 42-43). The binding agent is a biological molecule because the molecule is an oligonucleotide (page 50, lines 1-5) hybridized to a target DNA (page 50, lines 1-2). Thus, the claimed biomolecule is the double stranded (i.e., target/probe) DNA, which is a biological molecule, that is covalently linked to the surface. Paragraphs 0042-0044 of the instant specification recite embodiments wherein the biomolecules include, but are not limited to, DNA sequences. Further, a review of the specification yields no teaching excluding double stranded DNA sequences; thus, the claim has been given the broadest reasonable interpretation consistent with the teachings of the specification regarding a "biomolecule." Figures 2C-D of Fish further comprises nanotube 26 (i.e., a nanocylinder), having oligonucleotide 26b attached, which hybridizes to a single stranded portion of analyte 15a (second embodiment, pages 18-19). The hybridization is the specific binding between the overhang of the first biomolecule (i.e., the overhang on 15a of double stranded 16/15a) and complementary biomolecule 26b. Fish also teaches the covalent attachment of the

oligonucleotides 26a to the nanotube; namely, Figure 2F, which illustrates covalent linkage of amino terminal oligonucleotides to the end of the nanotubes (page 18, last two lines –page 19).

While Fish teaches both amine linkages to nanotubes (e.g., Figure 2F) and thiolated oligonucleotides (Example 1; page 56), Fish does not explicitly teach an amine-terminated nanocylinder with a molecule comprising a maleimide group and linkage of the maleimide group to a thiol group.

However, Strother et al teach attachment of biomolecules to surfaces using maleimide derivatives; e.g., Figure 1. Figure 1 shows a thiolated DNA attached to a maleimide moiety, which is further attached to a surface through an amine link and the junction between SSMCC and PL using the heterobifunctional cross linker SMCC (page 1206, column 2, first paragraph). Strother et al also teach the maleimide crosslinker SSMCC advantageously results in an activated surface that is coupled in aqueous solution to yield modified surfaces (page 1206, column 2, first paragraph). Thus, Strother et al teaches the known technique of linking an amine-terminated surface with a molecule comprising a maleimide group and linkage of the maleimide group to a thiol group on a biomolecule.

It would therefore have been obvious to a person of ordinary skill in the art at the time the claimed invention was made to have modified substrate comprising the amino terminal nanotubes linked to biomolecules as taught by Fish with the SSMCC linkage as taught by Strother et al to arrive at the instantly claimed substrate with a reasonable expectation of success. The modification would result in an amine terminated nanocylinder linked to a molecule comprising a maleimide group (i.e., claim 10), wherein the maleimide group is linked to a thiol terminated biomolecule (i.e., claim 11). The ordinary artisan would have been motivated to make such a modification because said modification would have resulted in a modified substrate having the added advantage of having an activated surface that is coupled under aqueous conditions as explicitly taught by Strother et al (page 1206, column 2, first paragraph). In addition, it would have been obvious to the ordinary artisan that the known technique of using the amino-maleimido-thiol linkage of Strother et al could have been applied to the substrate of Fish

with predictable results because the known technique of using the amino-maleimido-thiol linkage of Strother et al predictably result in stable association of biomolecules to surfaces.

Response to Arguments

Applicant's arguments on pages 11-12 of the Remarks regarding the previous rejection of claims 10-11 rely on arguments regarding the alleged deficiencies of Fish. These arguments are addressed above. Because the arguments regarding Fish were not persuasive, the rejections of claims 10-11 are maintained.

10. Claims 1 and 4 are rejected under 35 U.S.C. 103(a) as being unpatentable over Braun et al (PCT International Publication No. WO 99/04440, published 28 January 1999) in view of Jin et al (U.S. Patent No. 6,250,984 B1, issued 26 June 2004).

It is noted that this rejection applies to claim 1 to the extent that it is drawn to the embodiment of dependent claim 4.

Regarding claim 4, Braun et al teach the modified substrate of claim 1. In a single exemplary embodiment, Braun et al teach an interface component, which is an electrode (page 7). An oligonucleotide is attached to the surface of the electrode, and is used as a linker for binding to a nucleotide-chain end segment of a fiber (Figure 1B and page 22). This oligonucleotide linker hybridizes (i.e., to a complementary sequence; page 9, definition of a "linker") to complementary sequences on a fiber (page 15). Oligonucleotides are biomolecules, and the fiber has nucleotide chains at each of the ends of a carbon nanotube (page 32, second paragraph), which is a nanocylinder. Thus, the hybridization that connects the substrate bound oligonucleotide biomolecule to the nanocylinder-bound complementary nucleic acid biomolecule is the specific binding of the instant claim, and occurs without the use of a third biomolecule. The oligonucleotides are covalently linked to the surface and the nanocylinder; namely,

each of the biomolecules is bound to the respective substrate or nanocylinder, and Braun et al teach binding is covalent (page 5, definition of "binding").

While Braun et al teach nanocylinders in the form of carbon nanotubes (page 32, second paragraph), Braun et al do not teach the functionally equivalent gold and silver nanorods (i.e., nanotubes).

However, Jin et al teach the use of Au and Ag (i.e., gold and silver) nanotubes, which have the added advantage of being less susceptible to oxidation (column 5, line 60-column 6, line 10), which results in nanorods having longer lifetimes dues to the resistance to oxidation. Thus, Jin et al teach the known technique of using gold and silver nanorods.

It would therefore have been obvious to a person of ordinary skill in the art at the time the claimed invention was made to have modified the substrate comprising carbon nanorods (i.e., nanocylinders) as taught by Braun et al by substituting the functionally equivalent gold and silver nanorods of Jin et al to arrive at the instantly claimed substrate with a reasonable expectation of success. The ordinary artisan would have been motivated to make the modification because said modification would have resulted in a substrate having the added advantage of using nanorods having longer lifetimes dues to the resistance to oxidation as a result of using nanorods that are less susceptible to oxidation as explicitly taught by Jin et al (column 5, line 60-column 6, line 10). In addition, it would have been obvious to the ordinary artisan that the known technique of using the functionally equivalent gold and silver nanorods of Jin et al could have been applied in place of the carbon nanotubes of the substrate of Braun et al with predictable results because the functionally equivalent gold and silver nanorods of Jin et al predictably result in viable conductive nanorods.

11. Claims 1 and 10-11 are rejected under 35 U.S.C. 103(a) as being unpatentable over Braun et al (PCT International Publication No. WO 99/04440, published 28 January 1999) in view of Strother et al (J. Am. Chem. Soc., vol. 122, pages 1205-1209 (2000)).

It is noted that this rejection applies to claim 1 to the extent that it is drawn to the embodiments of dependent claims 10-11.

Regarding claims 10-11, Braun et al teach a modified substrate. In a single exemplary embodiment, Braun et al teach an interface component, which is an electrode (page 7). An oligonucleotide is attached to the surface of the electrode, and is used as a linker for binding to a nucleotide-chain end segment of a fiber (Figure 1B and page 22). This oligonucleotide linker hybridizes (i.e., to a complementary sequence; page 9, definition of a "linker") to complementary sequences on a fiber (page 15). Oligonucleotides are biomolecules, and the fiber has nucleotide chains at each of the ends of a carbon nanotube (page 32, second paragraph), which is a nanocylinder. Thus, the hybridization that connects the substrate bound oligonucleotide biomolecule to the nanocylinder-bound complementary nucleic acid biomolecule is the specific binding of the instant claim, and occurs without the use of a third biomolecule. The oligonucleotides are covalently linked to the surface and the nanocylinder; namely, each of the biomolecules is bound to the respective substrate or nanocylinder, and Braun et al teach binding is covalent (page 5, definition of "binding").

While Braun et al teaches both amine and thiol linkages and thiolated oligonucleotides (page 10, line 25-page 11, line 10), as well as maleimide groups (Figure 7B), Braun et al do not explicitly teach an amine-terminated nanocylinder with a molecule comprising a maleimide group and linkage of the maleimide group to a thiol group.

However, Strother et al teach attachment of biomolecules to surfaces using maleimide derivatives; e.g., Figure 1. Figure 1 shows a thiolated DNA attached to a maleimide moiety, which is further attached to a surface through an amine link and the junction between SSMCC and PL using the heterobifunctional cross linker SMCC (page 1206, column 2, first paragraph). Strother et al also teach the maleimide crosslinker SSMCC advantageously results in an activated surface that is coupled in aqueous solution to yield modified surfaces (page 1206, column 2, first paragraph). Thus, Strother et al teaches the

known technique of linking an amine-terminated surface with a molecule comprising a maleimide group and linkage of the maleimide group to a thiol group on a biomolecule.

It would therefore have been obvious to a person of ordinary skill in the art at the time the claimed invention was made to have modified substrate comprising the nanotubes linked to biomolecules as taught by Braun et al with the SSMCC linkage as taught by Strother et al to arrive at the instantly claimed substrate with a reasonable expectation of success. The modification would result in an amine terminated nanocylinder linked to a molecule comprising a maleimide group (i.e., claim 10), wherein the maleimide group is linked to a thiol terminated biomolecule (i.e., claim 11). The ordinary artisan would have been motivated to make such a modification because said modification would have resulted in a modified substrate having the added advantage of having an activated surface that is coupled under aqueous conditions as explicitly taught by Strother et al (page 1206, column 2, first paragraph). In addition, it would have been obvious to the ordinary artisan that the known technique of using the amino-maleimido-thiol linkage of Strother et al could have been applied to the substrate of Braun et al with predictable results because the known technique of using the amino-maleimido-thiol linkage of Strother et al predictably result in stable association of biomolecules to surfaces.

12. Claims 32-36 are rejected under 35 U.S.C. 103(a) as being unpatentable over Braun et al (PCT International Publication No. WO 99/04440, published 28 January 1999).

Regarding claim 32, Braun et al teach a nanocylinder bridge. In a single exemplary embodiment, Braun et al teach Figure 6, which comprises a first surface in the form of particle 600 having oligonucleotide 604 bound thereto (page 30). Figure 6 also shows a second surface in the form of electrode 610, which is bound to the fiber 614, wherein the fiber is a fiber of Figure 8A (page 30). Fiber 700 of Figure 8A has oligonucleotides 704 and 706 with nanotube 702 in between (page 32); thus, second surface 610 is attached to a fiber bearing a nanocylinder and two biomolecules in the form of oligonucleotides 704 and 706. Figure 6 further shows hybridization of the ends of the two

oligonucleotides, which is a specific binding between the biomolecules that forms a bridge between the two surfaces without a third biomolecule. Braun et al also teach the oligonucleotides are covalently linked to the surface and the nanocylinder; namely, each of the biomolecules is bound to the respective substrate or nanocylinder, and Braun et al teach binding is covalent (page 5, definition of "binding").

While Figure 6 of Braun et al shows first substrate 600 with biomolecule 604 specifically bound to a nucleic acid of fiber 614, wherein fiber 614 is has a second nucleic acid on the other end of the nanotube (e.g., Figure 8A), Braun et al do not specifically teach the second nucleic acid on the other end of the nanotube fiber is hybridized to a nucleic acid on second surface 610.

However, Braun et al also teach two substrates in the form of electrodes 300 of Figure 3A each having oligonucleotides 306 and 308 respectively attached, and connected by fiber 310 via specific binding of the oligonucleotides on the electrodes to complementary oligonucleotide strands on each end of the fiber (pages 24-25). Thus, Braun et al teach the known techniques of having two substrates each having an oligonucleotide attached thereto, wherein each oligonucleotide is hybridized to complementary oligonucleotides on the end of a fiber.

It would therefore have been obvious to a person of ordinary skill in the art at the time the claimed invention was made that the fiber 704 (of Figure 8A) connecting the two surfaces of Figure 6 could have been modified so that oligonucleotide 604 on the first surface 600 hybridizes with one of the oligonucleotides 704 or 706 on fiber 700, and that the other of oligonucleotides 704 or 706 on fiber 710 hybridizes to oligonucleotide 614 in order to form the bridge to second surface 610 in accordance with the fiber linkages described in Figure 3A to arrive at the instantly claimed invention with a reasonable expectation of success. The ordinary artisan would have been motivated to make such a modification because Braun et al teach the known technique of using oligonucleotide hybridization predictably results in a reliable method of connecting the ends of the fibers to their respective surfaces (e.g., Figure 6 and pages 24-25).

Alternatively, it would also have been obvious to a person of ordinary skill in the art at the time the claimed invention was made to have modified the embodiment of Figure 3A so that the fiber connecting oligonucleotide 306 on the first surface to oligonucleotide 308 is obvious variant fiber 700 of Figure 8A. The modification would result in oligonucleotide 306 hybridized to oligonucleotide 704 and oligonucleotide 608 hybridizing to oligonucleotide 706, thus making nanocylinder 702 a bridge between the two surfaces. The ordinary artisan would have been motivated to make such a modification because Braun et al teach the known technique of using the composite fibers of Figure 8A predictably results in a viable fiber for connecting surfaces (page 32).

Regarding claim 33, the bridge of claim 32 is discussed above. Braun et al teach the nanocylinder is a carbon nanotube (page 32, second paragraph).

Regarding claim 34, the bridge of claim 33 is discussed above. Braun et al also teach the two biomolecules on the carbon nanotube are at different ends of the nanotube (Figure 8A).

Regarding claim 35, the bridge of claim 32 is discussed above. Braun et al further teach the oligonucleotides on the different end of the nanocylinder are different (i.e., have different ends; page 30). Thus, they are not complementary to one another, as required by the claim. Alternatively, Braun et al also teach the two surfaces of Figure 3A are separately immobilized (i.e., wetted) with different oligonucleotides A and B (i.e., sequences 306 and 308). Thus, sequences 306 and 308 are different, which requires the complementary sequences on the ends of the nanocylinder to be different. Thus, they are not complementary to one another, as required by the claim.

Regarding claim 36, the bridge of claim 32 is discussed above. Braun et al teach the first and second surfaces are metal; namely, first surface 600 is a colloid particle made of metal (page 30) and second surface 610 is an electrode (page 30), which is also made of metal (page 24, last paragraph). Alternatively, Braun et al teach the two surfaces of Figure 3A are metal electrodes (pages 24-25).

12. Claim 37 is rejected under 35 U.S.C. 103(a) as being unpatentable over Braun et al (PCT International Publication No. WO 99/04440, published 28 January 1999) in view of Kuekes et al (U.S. Patent No. 6,128,214, issued 3 October 2000).

Regarding claim 37, Braun et al teach a surface. In a single exemplary embodiment, Braun et al teach an interface component, which is an electrode (page 7). An oligonucleotide is attached to the surface of the electrode, and is used as a linker for binding to a nucleotide-chain end segment of a fiber (Figure 1B and page 22). This oligonucleotide linker hybridizes (i.e., to a complementary sequence; page 9, definition of a "linker") to complementary sequences on a fiber (page 15). Oligonucleotides are biomolecules, and the fiber has nucleotide chains at each of the ends of a carbon nanotube (page 32, second paragraph), which is a nanocylinder. Thus, the hybridization that connects the substrate bound oligonucleotide biomolecule to the nanocylinder-bound complementary nucleic acid biomolecule is the specific binding of the instant claim, and occurs without the use of a third biomolecule. The oligonucleotides are covalently linked to the surface and the nanocylinder; namely, each of the biomolecules is bound to the respective substrate or nanocylinder, and Braun et al teach binding is covalent (page 5, definition of "binding").

While Braun et al teach a patterned surface in the form of a glass substrate having electrodes (i.e., a plurality) fabricated (i.e., patterned) thereon (Example 7), and while Braun et al teach the fibers function as molecular wires (pages 7-8, definition of "wire") and are part of a geometrical multidimensional network structure (page 7, definition of "network"), Braun et al do not explicitly teach a plurality of the wires (i.e., fibers) on a patterned substrate.

However, Kuekes et al teach the use of a two dimensional array (i.e., a patterned surface) comprising a plurality of nanometer-scale device, each having molecular wire structures therein (Abstract), which has the added advantages of ease of fabrication and allowing construction of a defect-tolerant interconnect network (column 2, lines 5-35). Thus, Kuekes et al teaches the known technique of a providing a plurality of molecular wires (i.e., fibers) on a patterned substrate.

It would therefore have been obvious to a person of ordinary skill in the art at the time the claimed invention was made to have modified patterned network comprising the molecular wires of nanotubes linked to biomolecules as taught by Braun et al into a plurality of molecular wires (i.e., fibers) on a patterned substrate as taught by Kuekes et al to arrive at the instantly claimed invention with a reasonable expectation of success. The ordinary artisan would have been motivated to make such a modification because said modification would have resulted in a modified substrate having the added advantages of ease of fabrication and allowing construction of a defect-tolerant interconnect network explicitly taught by Kuekes et al (column 2, lines 5-35). In addition, it would have been obvious to the ordinary artisan that the known technique of combining a plurality of molecular wires on a patterned substrate as taught by Kuekes et al could have been applied to the substrate of Braun et al with predictable results because the known technique of combining a plurality of molecular wires on a patterned substrate as taught by Kuekes et al predictably results in a viable arrangement of molecular switches.

Conclusion

13. No claim is allowed.

14. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Robert T. Crow whose telephone number is (571)272-1113. The examiner can normally be reached on Monday through Friday from 8:00 am to 4:30 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ram Shukla can be reached on (571) 272-0735. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Art Unit: 1634

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/Robert T. Crow/
Examiner, Art Unit 1634

/Diana B. Johannsen/
Primary Examiner, Art Unit 1634

Robert T. Crow
Examiner
Art Unit 1634